follow up period is 14 months. **Conclusion:** Our initial experience shows that allogeneic stem cell transplantation is an effective treatment option in patients of chronic myeloid leukaemia in chronic phase, who are less than 50 years of age and have HLA matched sibling donor. This is in line with experience from other centers.

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### PROGNOSTIC PROGENITOR PROFILING IN CHRONIC MYELOMONOCYTIC LEUKEMIA

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Chronic myelomonocytic leukemia (CMML) is a unique myeloproliferative disease characterized by marrow dysplasia and an increase in monocytes. The median survival of patients with CMML is short, in part, because CMML is frequently resistant to therapy. A better understanding of the basic biology of CMML progenitors is needed in order to reduce regimen related toxicity and provide more effective CMML targeted therapies. To this end, a mouse transgenic model of CMML was created in which human bcl-2 overexpression was targeted to the myeloid lineage by the myeloid promoter hMRP8. Transgenic hMRP8-bcl2 mice developed a myeloproliferative disorder characterized by a monocytosis in all hematopoietic tissues and splenomegaly. Myeloid progenitor analysis of hMRP8-bcl-2 bone marrow revealed a marked expansion of human bcl-2 expressing granulocyte-macrophage progenitors compared with control mice. In order to see if this correlated with human CMML, we used FACS analysis and recently identified phenotypic markers to identify phenotypic and functional differences between normal and CMML bone marrow hematopoietic stem cells and myeloid progenitors. CMML marrow was typified by a reduction in $CD34^+CD38^-CD90^+Lin^-$ hematopoietic stem cells and an expansion of $CD34^+CD38^-CD90^-Flk2^+Lin^-$ cells relative to normal bone marrow. In addition, there was a two-fold expansion in common myeloid progenitors (CMPs) and a corresponding decrease in megakaryocyte-erythroid progenitors (MEPs) suggesting that there was a skew in differentiation toward the myeloid lineage. In contrast to normal bone marrow derived CMPs, CMML CMPs gave rise to myeloid but not erythroid colonies. Moreover, real time quantitative RT-PCR analysis of highly purified FACS-sorted CMML CMPs demonstrated increased expression of two key regulators of myelomonocytic differentiation, PU.1 and c-jun, compared with normal bone marrow. A more detailed understanding of the basic biology of CMML progenitors and the genes that work in concert to expand them may aid in identifying novel molecular targets for CMML.

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### POST-REMISSION THERAPY OF ACUTE MYELOID LEUKEMIA IN FIRST REMISSION

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**Background:** At AML in first remission, treatment-modality depends on patient's prognostic factor and donor availability. According to the risk group of AML, post remission therapy has not established. We analyzed the effect of post-remission therapy of AML in first remission, allogeneic, autologous HSCT and intensive chemotherapy. **Method:** According to the post-remission therapy, we retrospectively evaluated the prognostic factor, the event-free survival (EFS) and the overall survival (OS) of 122 patients with AML in first remission from 1995 to 2004. All patients received standard induction therapy. After complete remission had been achieved, consolidation therapy was started. According to patients' clinical status and donor availability, patients were offered the different treatment-modalities, allogeneic, autologous HSCT or intensive chemotherapy. **Result:** Twenty-five patients received allogeneic HSCT, 36 patients autologous HSCT and 61 patients intensive chemotherapy. Median age was 33 years in allogeneic HSCT group, 38 years in autologous HSCT group, and 46 years in intensive chemotherapy group. The 5-year EFS were 72% in allogeneic HSCT group, 57% in the autologous HSCT group and 50% in chemotherapy group ($p=0.049$). When comparing between treatment groups, there was no difference in EFS. The 5-year OS rates were 80% in allogeneic HSCT group, 60% in autologous HSCT group and 53% in chemotherapy group ($p=0.02$). There was a significant difference in OS only between allogeneic HSCT group and chemotherapy group ($p=0.04$). There was an advantage in terms of EFS ($p=0.04$) and OS ($p=0.03$) with HSCT as compared intensive chemotherapy. The EFS and OS of allogeneic HSCT as compared with autologous HSCT has not difference. There was a significant benefit for EFS and OS with HSCT group when compared to those in intensive chemotherapy group in the high risk group of AML patients ($p<0.05$). In the intermediate and low risk group of AML, there was no significant difference in OS with HSCT as compared to the intensive chemotherapy, but a significant benefit for EFS of HSCT as compared with the intensive chemotherapy ($p<0.05$). **Conclusion:** The treatment of high risk-AML in first remission with either allogeneic or autologous hematopoietic stem cell transplantation prolongs EFS and OS as compared with intensive chemotherapy. In the intermediate or low risk-AML, there was a significant benefit for only EFS with HSCT compared as intensive chemotherapy.

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### ALLOGENEIC STEM-CELL TRANSPLANTATION IN PATIENTS WITH AML AND MDS USING MYELOABLATIVE VERSUS REDUCED-INTENSITY DOSES OF INTRAVENOUS BUSULFAN (BUSULFEX): THE ROLE OF DOSE INTENSITY

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Allogeneic stem cell transplantation (SCT) is a potentially curative approach in patients (pts) with AML and MDS. Intravenous busulfan (Busulfex, ivBu) reduces treatment-related mortality (TRM) and improves outcome after standard ablative conditioning. Reduced-intensity regimens allow SCT in pts not eligible for standard conditioning. It is not yet well established what are the dose intensities of ivBu predicting of better outcome in different settings. 91 pts were included in this analysis; median age 50 years (range, 18–70). 77 had AML (33 secondary) and 14 had MDS. The donors were HLA-matched siblings (n=45), 1-Ag mismatched relatives (n=6) or matched-unrelated (n=40). 42 pts were in first or second remission at SCT, or untreated with <10% marrow blasts; 49 were chemo-refractory or with >10% marrow blasts (active disease). 43 pts had ablative conditioning with ivBu, 12.8 mg/kg (Bu16) and cyclophosphamide (Cy). 48 pts considered not eligible for ablative therapy were given fludarabine (Flu) and escalated doses of ivBu, 6.4–12.8 mg/kg, (Bu8–16). With a median follow-up of 14 months, the 2-year overall (OS) of all pts was 48% (95 CI, 36–61). The cumulative incidence of TRM and relapse were 15% and 39%, respectively. The most important predictive factor for OS in multivariant analysis was active disease at SCT (HR 3.7, p=0.001). Age, gender, secondary AML/MDS, donor type and regimen used were not significant. There was no difference in OS between pts given different doses of ivBu. The OS of pts given Bu16 (with Cy or Flu) was 49%, compared with 51% in pts given Flu and Bu8–12. Pts given Bu16 had higher risk of TRM (19% vs 7%) and lower relapse rate (34% vs 46%), not reaching statistical significance. However, ivBu dose had a significant influence in pts with active disease. OS, TRM and relapse rates were 45%, 22%, and 34% in pts given Bu16 compared with 0% (p=0.05), 18% (p=NS), and 82% (p=0.04) after Bu8–12, respectively. In conclusion, ivBu containing regimens are well tolerated with relatively low TRM rates. Dose intensity is not predictive of outcome in chemo-sensitive disease. However, pts with active disease could only be salvaged if given ablative doses of ivBu. Pts considered not eligible for ablative conditioning tolerated Flu and ablative doses of ivBu relatively well, and could be salvaged with this regimen even when treated for active disease. Randomized studies will be needed to further determine the best dose-intensity in each setting.